## REMARKS

***Overview***

In the Office Action under reply, claims 1-3, 5-25, and 27-33 are pending, claims 4 and 26 having been previously canceled. The pending claims have been rejected as follows:

(1) claims 1-3, 5-25, and 27-33 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement;

(2) claims 1, 3-6, 8, and 10-13 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite; and

(3) claims 1-3, 5-25, and 27-33 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.

These rejections are addressed in part by the amendments made herein, and are otherwise traversed for the reasons set forth below.

***Claim Amendments***

By the amendments made herein, claims 1, 2, 8, 19-22, and 32 have been amended to specify that the cyclic ether group is a crown ether. Claims 1 and 19 have also been amended to state that the crown ether group has four or more oxygen atoms. Support for these amendments may be found, for example, in original paragraph [0021].

Claims 1 and 19 have also be amended to specify that the acidic group is selected from a benzoic acid group and a sulfonic acid group. Support for benzoic acid is found, for example, in paragraph [0023]. Support for sulfonic acid is found, for example, in paragraphs [0005] and [0055], which reference Tsaprailis et al. (1999), *J. Am. Chem. Soc.*, 121:5142. Tsaprailis et al. is incorporated by reference and discloses the following:

> The influence of acid-base interactions on the gas-phase dissociation of a series of protonated peptides was investigated. Peptides containing both acidic residues [aspartic (D), glutamic (E), and cysteic acid (C*)] and basic residues [arginine (R)] were dissociated by different activation methods that allow different time frames for dissociation.

(See Abstract.) Applicants note that cysteic acid contains a sulfonic acid group. In addition, the *Kirk-Othmer Encyclopedia of Chemical Technology*, incorporated by reference in paragraph [0042] of the application, contains an extensive article on sulfonic acids (a sample page from this reference is attached as Appendix A). Reference to matter in a document incorporated by reference is legitimate as explained by the MPEP:

> Instead of repeating some information contained in another document, an application may attempt to incorporate the content of another document or part thereof by reference to the document in the text of the specification. The information incorporated is as much a part of the application as filed as if the text was repeated in the application, and should be treated as part of the text of the application as filed.

(MPEP § 2163.07(b).)

Claim 1 has also been amended to specify that the transition metal binding group is a polyamine. Support for this amendment is found, for example, in originally filed claim 5.

Claim 1 has also been amended to specify that the transition metal binding group is selected from ethylenediamine, propylenediamine, butanediamine, hexamethylenediamine, N,N-dimethylethylenediamine, diethylenetriamine, dipropylenetriamine, triethylenetetramine, tetramethylethylenediamine, N,N-dimethylpropylenediamine, N,N,N'-trimethylethylenediamine, N,N,N',N'-tetramethyl-1,3-propanediamine, hexamethylenetetramine, diazabicyclononane, sparteine, phenantroline, 2,2'-bipyridine and neocuproine, and further amended to remove the phrase "alkyls, heteroalkyls, alkenyls, heteroalkenyls, aryls, heteroaryls, alkaryls, and alkheteroaryls."

In light of the aforementioned claim amendments, claims 5 and 27 have been canceled.

No new matter has been added by these amendments. Applicants note that the claim amendments are made without prejudice and for the sole purpose of expediting prosecution. Applicants hereby reserve the right to prosecute canceled subject matter in one or more divisional applications.

***First rejection under 35 U.S.C. §112, first paragraph***

Claims 1-3, 5-25, and 27-33 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. This rejection is traversed.

The Action acknowledges that the specification is enabling for benzoic acid, ethylenediamine, propylenediamine, butanediamine, hexamethylenediamine, N,N-dimethylethylenediamine, diethylenetriamine, dipropylenetriamine, triethylenetetramine, tetramethylethylenediamine, N,N-dimethylpropylenediamine, N,N,N'-trimethylethylenediamine, N,N,N',N'-tetramethyl-1,3-propanediamine, hexamethylenetetramine, diazabicyclononane, sparteine, phenantroline, 2,2'-bipyridine and neocuproine transition metal binding groups, diazo groups, and compounds 1-5 (Action at 2). The groups identified as enabled are specifically called

out in paragraphs [0023], [0026], and [0029] of the original specification. Applicants strongly object to the implication that the skilled artisan would not be able to extend the teachings of the application to any groups not specifically mentioned in the application, no matter how similar they may be to the non-limiting examples provided. This implication is inconsistent with the state of the art of chemistry, and is also inconsistent with the MPEP and case law.

Nevertheless, in the interest of speeding prosecution, applicants have narrowed the scope of the claims to comply with many of the Examiner's suggested claim amendments.

In particular, applicants have amended claim 1 to recite the transition metal binding groups listed in the Action.

Applicants have further amended claim 1 to recite that the cyclic ether must be a crown ether having four or more oxygen atoms. This amendment narrows the scope of the claims, since crown ethers are a subset of cyclic ethers. The term "crown ether" is an art-recognized term, indeed one which is taught in college organic chemistry textbooks such as T.W. Graham Solomons, *Organic Chemistry* (6th ed. 1996). In fact, the 1987 Nobel Prize in Chemistry was awarded to Charles Pedersen for his development of crown ethers. The limitation of having four or more oxygen atoms provides additional guidance to delineate the scope of the claims. Based on the disclosure, the skilled artisan would be capable of incorporating the full range of crown ethers into the compounds encompassed by the claims. For example, given synthetic details for synthesizing a compound comprising an 18-crown-6 moiety, it is not a mystery to the skilled artisan to incorporate 12-crown-4, or 30-crown-10, or aza-18-crown-6 into the compound. See, for example, Julian et al. (2002), *J. Am. Soc. Mass Spectrom.*, 13:493-498, cited previously in an Information Disclosure Statement (IDS) dated August 18, 2004, as well as Julian et al. (2004), *J. Am. Soc. Mass Spectrom.*, 15:616-624, cited in the IDS accompanying this submission. Extension of the synthetic procedures of the disclosure to alternative crown ethers is well within the skill in the art, and a large number of journal articles are readily available to assist the skilled artisan with such substitution. Accordingly, the disclosure is sufficient to enable the skilled artisan to make and use the claimed invention with respect to crown ethers.

Applicants have further amended claim 1 to recite that the acidic group is selected from a benzoic acid group and a sulfonic acid group. The use of sulfonic acid groups in the claimed compounds is supported by the reference Tsaprailis et al. (1999), *J. Am. Chem. Soc.*, 121:5142,

which is incorporated by reference in the specification (e.g., paragraph [0055]). Tsaprailis et al. states, for example, that

> the peptide incorporating a cysteine residue yields limited fragmentation at low collision energies and an extensive series of abundant sequence-specific b-, a-, and y-type ions in addition to low-*m/z* immonium product ions at collision energies > 70 eV.... It should be noted that the aggregate loss of H2SO3 (leading to characteristic ions such as bn-H2SO3; Figure 1B) is further supporting evidence of the chemical modification (i.e., oxidation) in the peptides...

[Tsaprailis et al., p 5146.] Furthermore, and as with crown ethers, the skilled artisan would be able to apply the teachings of the specification to numerous acids, including sulfonic acid. See, for example, Keough et al. (2003), *Analytical Chem.*, 75(7):156A-165A (copy provided in the accompanying IDS), which describes the use of sulfonic acid derivatives for cleaving peptide bonds.

The Action points to *In re Wands* cited in MPEP 2164.01(a) as providing the standard for enablement (Action at 3). Applicants point out that the MPEP also discusses *In re Wands*:

> In *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), the court reversed the rejection for lack of enablement under 35 U.S.C. 112, first paragraph, concluding that undue experimentation would not be required to practice the invention.... The court found that the specification provided considerable direction and guidance on how to practice the claimed invention and presented working examples, that all of the methods needed to practice the invention were well known, and that there was a high level of skill in the art at the time the application was filed. Furthermore, the applicant carried out the entire procedure for making a monoclonal antibody against HBsAg three times and each time was successful in producing at least one antibody which fell within the scope of the claims.

(MPEP § 2164.06(b).) In the instant case, undue experimentation would not be required to extend the teachings of the specification (i.e., the specific groups listed in the Action) to compounds containing a variety of crown ethers as well as compounds containing sulfonic acid groups. The skill in the art is high, and synthetic procedures for incorporating such groups are described in the specification or known in the art.

Applicants stress that the claims have been narrowed to closely resemble the subject matter that the Examiner acknowledges is enabled. In light of the foregoing arguments and the claim amendments made herein, the disclosure fully enables the claims, and applicants respectfully request withdrawal of the rejection.

***Rejection under 35 U.S.C. §112, second paragraph***

Claims 1, 3-6, 8, and 10-13 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. The Action focuses on the identifiability of various claimed groups, including those described using the words "heteroaryl" and "heterocyclic." Although applicants disagree with the assertions set forth in the Action, applicants believe that, in light of the amendments set forth herein, this rejection is moot.

Regarding "crown ethers," the Examiner previously objected to the term as indefinite (see Office Action dated 12/22/06 at p. 2) because the claims did not also recite the limitation of having four or more oxygen atoms. In light of the amendments made herein, applicants believe that the Examiner's concern for this term is also satisfied.

Applicants note that "[t]he test for definiteness under 35 U.S.C. 112, second paragraph, is whether 'those skilled in the art would understand what is claimed when the claim is read in light of the specification.' *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986)." (MPEP § 2173.02.) Because each of the terms in the claims is well known in the art and/or defined in the specification, it is clear that the skilled artisan would be capable of understanding that which is being claimed.

Applicants stress that the words identified in the Action as "not identifiable" have been removed from the claims, and the claims have been narrowed so that the limiting elements do not have "voluminous complex meanings" (Action at 4). In light of the claim amendments made herein, applicants respectfully request withdrawal of the rejection.

***Second rejection under 35 U.S.C. §112, first paragraph***

Claims 1-3, 5-25, and 27-33 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. This rejection is overcome by the amendments set forth herein and otherwise traversed.

The Action states that the issue pertaining to written description is over the meaning of the phrases "amine group containing compounds, cyclic ether, acidic groups, transition metal binding groups and diazo groups," discussed in connection with enablement. Although applicants disagree with the assertions set forth in the Action, applicants believe that the narrowing amendments set forth herein should overcome this concern. In particular, applicants point out that each of the abovementioned terms are present in the claims (as amended herein) with limitations that narrow their scope. The specification provides sufficient written description for

these narrowed terms, as the skilled artisan would have no difficulty in identifying the scope of the terms and that applicants had possession of the claimed invention at the time of filing.

The Action also objects to the lack of a "complete generic formula" in the rejected claims (Action at 7). The rejection presupposes that a formula is required for applicants to satisfy the written description requirement. This position is not supported by the relevant statute or case law. As stated in the MPEP:

> ...the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)... Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.

(MPEP §2163.02, emphasis added.) The presence of chemical formulas is one way to satisfy the written description requirement, but it is clearly not the only way or a prerequisite for satisfying the requirement. The invention may be described *in any way* that demonstrates applicants' possession of the invention as claimed. Describing actual preparations of the claimed compositions is one such way, as is identifying characteristics sufficient to show that the applicants were in possession of the claimed invention.

In this case, words such as "amine-group containing" are used instead of an explicit formula in some cases. However, persons of skill in the art would immediately understand that "amine-group containing" connotes the same thing as the formulas $RNH_2$, $R^1R^2NH$, and $R^1R^2R^3N$. The words connote structure just as precisely as formulas would. The same is true for "diazo," for example, which immediately brings to mind the formula $R^1R^2C{=}N_2$.

The Action states that "[t]he claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art" (Action at 7). It is not clear what the Examiner has in mind as an "essential or critical feature." To the extent the Examiner has in mind a formula as the "essential or critical feature," applicants disagree with this interpretation. One of skill in the art would understand that there are only a finite number of plausible ways in which the claimed groups can be incorporated into a compound as recited in the claims, and the example chemical structures (i.e., structures 1-5)

provided in the specification are sufficient to show the skilled artisan that applicants were in possession of the claimed invention.

The Action cites *Regents of the Univ. of Cal. v. Eli Lilly and Co.*, 119 F.3d 1559 (Fed. Cir. 1997) as holding that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name' of the claimed subject matter sufficient to distinguish it from other materials" (Action at 8). The opinion in *Regents v. Eli Lilly* actually supports applicants' position insofar as it recognizes that a chemical name or structure is as effective in providing written description as a formula. Furthermore, the genus at issue in *Regents v. Eli Lilly* was one of DNA molecules. The opinion cites *Fiers v. Revel*, 984 F.2d 1164 (Fed. Cir. 1993). The court in *Fiers* was also referring specifically to written description requirements for DNA: "If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name, or physical properties, as we have held, then a description also requires that degree of specificity." (*Id.* at 1171.) The test for adequate written description should reflect the disparity in complexity between DNA molecules with molecular weights in the millions of daltons and the compounds of the present claims.

Second, and particularly in light of the amendments that are set forth herein, applicants believe that the claims are fully supported by adequate written description. The individual groups currently recited in the claims are clearly delineated and are well known groups in the art. The skilled artisan requires no more than the phrase "crown ether group containing four or more oxygen atoms" in order to envision the scope of groups that fall within such a limitation. The same argument also applies to diazo groups. Furthermore, the terms benzoic acid, sulfonic acid, and the various transition metal binding groups recited in the claims as currently amended each refer to specific groups that are known in the art and completely described by the respective terms. Adequate written description is provided for these groups simply by providing their names. Finally, given any particular compound the skilled artisan would be capable of determining whether the compound is "an amino acid, a peptide, or a protein" as required by the claims. Because such compounds are so well known in the art, the skilled artisan would have understood that applicants were in possession of the invention defined by the pending claims at the time the invention was made.

The Action states that

> [t]he terms [amine containing compounds, crown ether, acidic groups, transition binding groups, and diazo groups] do not bring to mind a particular structure. It is important whether the term is one that is understood to describe structure, as opposed to a term that is simply a nonce phrase or a verbal construct that is not recognized as the name of structure and is simply a substitute for the term 'means for.'

(Action at 9.) Applicants stress that each of the terms objected to (i.e., amine containing compounds, crown ether, acidic groups, transition metal binding groups, and diazo groups) are now further described in the claims by purely structural limitations. Thus, amine containing compounds are amino acids, peptides, or proteins, each of which denotes a particular and well established structure. Crown ethers are also well established groups that have a readily identifiable structure. Acidic groups in the claims are limited to either benzoic acid or sulfonic acid groups, both of which provide well-defined structural limitations. Transition metal binding groups are ethylenediamine, propylenediamine, butanediamine, hexamethylenediamine, N,N-dimethylethylenediamine, diethylenetriamine, dipropylenetriamine, triethylenetetramine, tetramethylethylenediamine, N,N-dimethylpropylenediamine, N,N,N'-trimethylethylenediamine, N,N,N',N'-tetramethyl-1,3-propanediamine, hexamethylenetetramine, diazabicyclononane, sparteine, phenantroline, 2,2'-bipyridine and neocuproine, each of which has a well defined structure. Diazo groups are groups containing ($=N_2$), as stated in paragraph [0029] of the original specification. Each of the terms in the claims therefore refer to well defined structural features, and none of the terms may be construed as a simple substitute for a "means for" limitation (i.e., a limitation free of any structural component). The combination of the structural limitations found in the pending claims, read in light of the specification, provides adequate written description such that the skilled artisan is instantly able to determine whether a particular compound falls within the scope of the claims.

In light of the arguments set forth herein and the amendments to the claims, applicants submit that the claims comply with the written description requirement under 35 U.S.C. §112, first paragraph. Accordingly, applicants respectfully request withdrawal of the rejection.

## CONCLUSION

Applicants submit that the claims of the application are in condition for allowance. Applicants respectfully request withdrawal of the rejections, and prompt issuance of a notice of allowance. If the Examiner has any questions concerning this communication, or would like to discuss the application, the art, or other pertinent matters, a telephone call to the undersigned would be welcomed.

Respectfully submitted,

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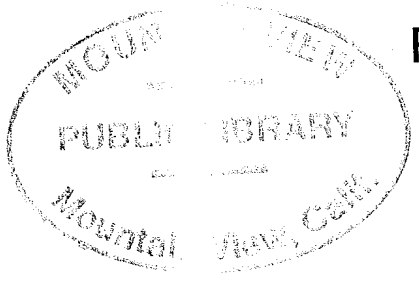
# Appendix A

*Kirk-Othmer Encyclopedia of Chemical Technology*, 4th Ed., Vol. 23, p. 194.

KIRK-OTHMER

# ENCYCLOPEDIA OF CHEMICAL TECHNOLOGY

FOURTH EDITION

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# SULFONIC ACIDS

Sulfonic (or sulphonic) acids are classically defined as a group of organic acids which contain one or more sulfonic, $-SO_3H$, groups. The focus of this chapter is an overview of organic sulfonic acids which have the formula $RSO_3H$, where the R-group may be derived from many different sources. Typical R-groups are alkane, alkene, alkyne, and arene. The R-group may contain a wide variety of secondary functionalities such as amine, amide, carboxylic acid, ester, ether, ketone, nitrile, phenol, etc. Sulfonic acid derivatives are used industrially on a large scale in the manufacture of surfactants, dyes, inks, dispersing agents, and polymers. Sulfonic acids also find broad application as catalysts in both alkylation (qv) processes and general organic reactions. Sulfonic acid derivatives have found more esoteric applications in the areas of custom organic syntheses and biological research. Sulfonic acids derivatives, where the R-group is derived from an inorganic source such as a halide, oxygen (ie, sulfate), or amine (ie, sulfamic acid), are not discussed herein to a great extent. These last are often referred to as sulfuric acid derivatives (see CHLOROSULFURIC ACID).

## Physical Properties

The physical properties of sulfonic acids vary greatly depending on the nature of the R-group. Sulfonic acids are found in both the solid and liquid forms at room temperature. No examples of gaseous sulfonic acids are known as of the mid-1990s. Sulfonic acids can be described as having similar acidity characteristics to sulfuric acid. Sulfonic acids are prone to thermal decomposition, ie, desulfonation, at elevated temperatures. However, several of the alkane-derived sulfonic acids show excellent thermal stability, as shown in Table 1. Arene-based sulfonic acids are thermally unstable. These must be distilled under extreme vacuum

**Table 1. Physical Properties of Sulfonic Acids[a]**

| Acid | CAS Registry Number | Mp, °C | Bp,[b] °C | Density $d_4^{25}$, g/cm$^3$ |
|---|---|---|---|---|
| methanesulfonic acid | [*75-75-2*] | 20 | 122 | 1.48 |
| ethanesulfonic acid | [*594-45-6*] | −17 | 123 | 1.33 |
| propanesulfonic acid | [*28553-80-2*] | −37 | 159 | 1.19 |
| butanesulfonic acid | [*30734-86-2*] | −15 | 149 | 1.19 |
| pentanesulfonic acid | [*35452-30-3*] | −16 | 163 | 1.12 |
| hexanesulfonic acid | [*13595-73-8*] | 16 | 174 | 1.10 |
| benzenesulfonic acid | [*98-11-3*] | 44 | 172[c] | |
| *p*-toluenesulfonic acid | [*104-15-4*] | 106 | 182[c] | |
| 1-naphthalenesulfonic acid | [*85-47-2*] | 78 | dec | |
| 2-naphthalenesulfonic acid | [*120-18-3*] | 91 | dec | 1.44 |
| trifluoromethanesulfonic acid | [*1493-13-6*] | none | 162[d] | 1.70 |

[a] Refs. 1 and 2.
[b] At 133 Pa (1 mm Hg) unless otherwise noted.
[c] At 13.3 Pa (0.1 mm Hg).
[d] At 101.3 kPa = 760 mm Hg.